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| APPLICATION NO | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO | CONFIRMATION NO |
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| 09/509,559 | 11/27/2000 | Wolf-Georg Forssmann | P65315US0 | 8027 |

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| EXAMINER |
|---|
| DEBERRY, REGINA M |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1647 | |

DATE MAILED: 10/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Application No. | Applicant(s) |
|---|---|
| 09/509,559 | FORSSMANN ET AL. |
| **Examiner** | **Art Unit** |
| Regina M. DeBerry | 1647 |

## *Office Action Summary*

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *02 August 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *5-8,10,13 and 15-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,9,11,12,14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-18* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and or 121.

**Attachment(s)**

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 19
4)☐ Interview Summary (PTO-413) Paper No(s). __
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other

***Status of Application, Amendments and/or Claims***

The amendment filed 14 April 2000 (Paper No. 8) has been entered in full. The information disclosure statement filed 20 March 2001 (Paper No. 10) was received and complies with the provisions of 37 CFR §§1.97 and 1.98. It has been placed in the application file and the information referred to therein has been considered as to the merits. The amendment filed 26 September 2001 (Paper No. 13) has been entered in full. The amendment filed 08 March 2002 (Paper No. 18) has been entered in full. The amendment filed 26 April 2002 (Paper No. 21) has been entered in full.

Applicant's election with traverse of Group I (claims 1-4, 9, 11, 12 and 14) and SEQ ID NO:10 (peptide OB-CDGF) in Paper No. 23 (02 August 2002) is acknowledged. The traversal is on the grounds that PTO cannot require dividing a proper generic claim based on a restriction or election of species and further to the extent that, upon allowance of a generic claim, Applicants are entitled to claim a reasonable number of species in addition to the elected species.

Contrary to Applicant's assertion, the instant sequences are drawn to various human cadherin peptides. Different sequences constitute different products because they constitute diverse coding regions and/or impart structural and functional differences. PCT Rules provide for examination of one product, one method of making the product and one method of using the product.

The requirement is still deemed proper and is therefore made FINAL. Claims 5-8, 10, 13 and 15-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group, there being no allowable generic or

linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 23.

### *Claim Objections*

Claim 4 is objected to because of the following informalities: Claim 4 encompasses non-elected inventions and requires amendment to limit to elected invention. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Appropriate correction is required.

### *Claim Rejections - 35 USC § 101*

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-4 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 1-4 are directed to products that are not distinguished from peptides found in nature. Products of nature do not constitute patentable subject matter. Amending the claims to specify that the claimed peptides are "isolated" or "purified" is one way the instant rejection can be obviated.

Claim 12 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under

35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 9, 11, 12 and 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a peptide referred to as cadherin-derived growth factor (CDGF) consisting of SEQ ID NO:10, characterized by being a peptide cleaved off as a pro sequence during the processing of pro-cadherin into cadherin, and that said peptide has cell proliferative properties on osteoblasts and methods of administering CDGF consisting of SEQ ID NO:10 to promote bone growth does not reasonably provide enablement for the claims as recited. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-3 are drawn to the CDGF peptide of SEQ ID NO:10 and generic variants thereof. Claims 9 and 11 are drawn to medicaments comprising CDGF, claim 12 is drawn to a therapeutic method of administering CDGF to treat a variety of diseases and claim 14 is drawn to a process for the preparation of CDGF. The instant specification teaches that OB-CDGF (SEQ ID NO:10) has proliferation activity on

primary osteoblast (e.g. Example 1). The specification, however, fails to establish that OB-CDGF has cell-protective or cell-differentiation properties. For example, BR-CDGF (SEQ ID NO:12) and CAD 6-CDGF (SEQ ID NO:7) are disclosed as having activity on primary nerve cell cultures. The scope of patent protection sought by Applicant as defined by the claims fails to bear a reasonable correlation with the scope of enabling disclosure set forth in the specification for the following reasons.

The specification is not enabled for fragments or variants of SEQ ID NO:10. It is known for nucleic acids as well as proteins, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many cases (Wells, 1990, Biochemistry 29:8509-8517). The disclosure provides no guidance as to which regions of the CDGF peptide would be tolerant of modification while still maintaining the functional properties (cell proliferation) and it provides no working example of any variant sequence which would be within the claims.

Claim 12 is directed to a therapeutic method of administering CDGF to treat a wide variety of diseases. The specification only establishes that OB-CDGF (SEQ ID NO:10) has proliferative activity for osteoblasts. This activity is not predictive of the activity OB-CDGF might have against non-osteoblast cells and tissues, such as those recited in claim 12.

Due to the large quantity of experimentation necessary to generate the fragments or variants recited in the claims and screen same for cell proliferation activity, the large quantity of experimentation necessary to show a correlation between the instant invention and treatment of the diseases/conditions recited, the lack of

direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 9, 11, 12 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4 and 9 are indefinite because it is unclear whether "having" and "containing" are open or closed language.

Claim 9 is indefinite. The term "usual" is vague, therefore the metes and bounds of the claim cannot be determined.

Claim 11 is indefinite. The term "suitable" is vague, therefore the metes and bounds of the claim cannot be determined.

Claims 11,12 and 14 are improper Markush groups.

Claim 12 provides for the use of the medicament, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process

applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Regarding claim 12, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The instant method claim is missing key steps that determine how CDGF is prepared and whether the claim is open or closed. The following is an example of how the claim should be written. The omitted steps are: "wherein CDGF is prepared by processes comprising isolation" or "wherein CDGF is prepared by processes consisting of isolation".

Regarding claim 14, the phrase "per se" renders the claim indefinite.

### *Claim Rejections - 35 USC § 102*

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-4, 12 and 14 are rejected under 35 U.S.C. 102(e) as being anticipated Takeshita *et al.* Claim 4 is drawn to a CDGF having the sequence in SEQ ID NO:10. Takeshita teaches a bone related cadherin like protein that comprises the instant sequence (abstract and column 41, residues 26-51). The sequence of Takeshita is 100% identical to the instant sequence. Please see sequence query, Appendix A.

Claims 1-3 are rejected because the activities of CDGF are inherent. Claims 9 and 11 are rejected because intended use has not weight. Takeshita teaches that OSF-4 or its fragments can be produced by genetic engineering techniques or chemical peptide synthesis (column 1, lines 34-55), extracted from bone tissue (column 3, lines 52-61), and reproduced by recombinant techniques using expression vectors (example 8). Takeshita teaches that the substance can be used in treatment of various bone diseases (column 3, lines 1-3 and column 10, lines 41-45).

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (703) 305-6915. The examiner can normally be reached on Mondays-Fridays 8:00 a.m. - 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

RMD
October 8, 2002